DETAILED ACTION

1. Claims 7-10, 13-15, 36, 37, 39-50 are pending in the application.

2. In the prior action, mailed on October 12, 2007, claims 7-16, 24, and 26-39 were pending in the application; with claims 7-15 and 35-39 under consideration and rejected; and claims 24 and 26-34 withdrawn as to non-elected invention.

3. In the Response of February 12, 2008, the Applicant cancelled claims 11, 12, 16, 24, 26-35, and 38; amended claims 7, 8, 13 -15, 36, and 37; and added new claims 40-50.

4. Claims 45-50 are withdrawn as directed to a non-elected species.

5. Claims 7-10, 13-15, 36, 37, 39-44 are under consideration.

Information Disclosure Statement

6. Applicant's submission of the missing references from the September 2004 IDS is noted. However, the determination as to whether an IDS is compliant with the patent rules is based upon the contents of the IDS at the time of its filing. See e.g., MPEP 609.05(a). Thus, the later submission of the references does not bring the previously filed IDS into compliance. These references have therefore not been considered.

Drawings

7. **(Prior Objection- Restated)** The drawings were objected to because portions of Figure 8 are illegible. In view of the submission of a replacement copy of the Figure, the objection is withdrawn.

However, the replacement copy of Figure 8 has been modified such that the placement of the numbers relating to the positions of the provided sequence have been changed. Previously, the numbers appeared to indicate the position number of the first nucleic acid base in each line, and, as amended, currently appears to indicate the position number of the last nucleic acid residue. However, the same numbers are used in both the previous and the current version of the figure. This change of position therefore changes the definition of the disclosed sequence (thereby creating New Matter), and creates uncertainty in the interpretation of the specification. The replacement copy of Figure 8 is therefore objected to.

Claim Rejections - 35 USC § 112

8. **(Prior Rejection- Withdrawn)** Claims 13-16 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the amendments to the claims, the rejection is withdrawn.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. **(Prior Rejection- Withdrawn)** Claims 13-16 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. In view of the amendments to the claims, the rejection is withdrawn.

11. **(New Rejection- Necessitated by Amendment)** Claims 7-10, 13, 14, 15, 36, 37, 39, and 40-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to isolated nucleic acid molecules (and vectors comprising such) wherein the nucleic acids encode MLV ecotropic envelope proteins having a heterologous short peptide inserted within either the N-terminal or variable region of the extracellular domain, and wherein a chimeric retrovirus comprising the encoded envelope protein is capable of infecting a human cell, but not a mouse cell.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would

recognize from the specification the scope of what is being claimed. However, it is noted that the presence of multiple species with in a claimed genus does not necessarily demonstrate possession of the genus. See, In re Smyth, 178 U.S.P.Q. 279 at 284-85 (CCPA 1973; and University of California v. Eli Lilly and Co., 43 USPQ2d 1398, at 1405 (Fed Cir 1997)(citing Smyth for support). This is particularly the case where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated.

In the present case, the application identifies certain modified MLV envelope proteins which meet the structural and functional requirements of the claims. See e.g., page 20, lines 21-31. Thus, the application provides examples of species that fall within the claimed genus of nucleic acids.

However, it is noted that the application teaches that not every nucleic acid that meets the structural requirements of the claims also meets the functional requirements. This is because, on page 20, the application also teaches that while some heterologous peptide insertions result in envelope proteins conferring the required functions, others result in viruses that are able to infect neither human or murine cell, and others in viruses that are able to infect both. Moreover, the category into which the resulting virus falls does not appear to correlate predictably with any of the position of the insertion, or the peptide being inserted. Thus, while the application provides examples of species within the claimed genus, the teachings of the application also demonstrate uncertainty as to what other peptides may be inserted at what positions to result in nucleic acids that meet the functional, as well as the structural, requirements of the claims. In view of the uncertainty as to the operability of other undisclosed species, and the fact that the disclosed species relate to only a few potential positions and only two of the innumerable potential

heterologous peptides, the disclosed species are not found to be sufficiently representative of the claimed genus as a whole.

It is noted that the claims provide for both a structure and a function. However, as was described above, the teachings in the application demonstrate that the general structural feature of inserting any heterologous peptide into any N-terminal or variable region position of the SU domain of the MLV ecotropic envelope protein does not correspond to or correlate with the required function of the claims. Thus, the provision of the structure and function in the claim also fails to demonstrate descriptive support for the claimed genus as the structure does not correlate with the presence of the function.

Claim Rejections - 35 USC § 102

12. **(Prior Rejections- Withdrawn)** Claims 7, 8, 10, 11, 35-37, and 39 were rejected under 35 U.S.C. 102(b) as being anticipated by Wu et al. (Virology, 269:7-17). Claims 7, 8, 35-37, and 39 were rejected under 35 U.S.C. 102(b) as being anticipated by Kingsman (U.S. 6,132,731). Claims 7, 8, 35, 37, and 38 were rejected under 35 U.S.C. 102(e) as being anticipated by Albritton et al. (U.S. 6,448,390). The claims have been amended to add an additional functional limitation which, as pointed out by the Applicant, has not been shown by the cited prior art. The rejections are therefore withdrawn.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. **(Prior Rejections- Withdrawn)** Claims 9, 10, 11, and 13-16 were rejected under 35 U.S.C. 103(a) as being unpatentable over Albritton as applied to claims 7, 8, 35, 37, and 38 above. Claims 9-11, 13-15, and 39 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kingsman as applied against claims 7, 8, 35-37, and 39 above, and further in view of Anderson et al. (U.S. 5,985,655). The claims have been amended as described above. In view of the amendment, the rejection is withdrawn.

15. **(Prior Rejection- Maintained)** Claims 9-15 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kingsman as applied against claims 7, 8, 35-37, and 39 above, and further in view of Paul et al. (U.S. 5,736,387) and Panda et al. (Virology 273:90-100). Claim 12, which read on viral vectors comprising the nucleic acid of claim 7 which were not capable of infecting murine cells. Claim 7 was amended, as described above, to read on nucleic acids that encode mutant MLV ecotropic envelope proteins, wherein chimeric retroviruses comprising such encoded proteins are able to infect human, but not murine cells. In view of the amendment to the claims, the rejection is withdrawn from cancelled claims 11 and 12, but is extended to amended claims 7, 8, 36, 37, and 39 in addition to claims 9, 10, and 13-15. In addition, the rejection is also extended to new claims 40-44 have been added to the application. The rejection is therefore maintained over claims 7-10, 13-15, 36, 37, and 39-44.

The Applicant traverses the rejection of record on the basis that the teachings of Paul and Panda fail to remedy the deficiencies of Kingsman with respect to the cells that may be infected by retroviral particles comprising the encoded envelope protein of claim 7. These arguments are not found persuasive. The Applicant asserts that Paul only discloses viruses that infect mouse cells. While this may be the case, it was noted in the prior action that the reference does suggest in column 18 the additional modification of the viruses such that they do not do so. Further, the teachings of Panda indicate that those in the art would have known how to make such modifications.

Applicant's argument that Panda does not teach the modification of MLV particles such that they can infect human cells is also not found persuasive. It is noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). As the present rejection is not based on the teachings of this reference alone, but on what would have been obvious to those of ordinary skill in the art from the combination of the cited references the argument that Panda fails to teach each of the claim limitations is not found persuasive.

With respect to new claims 40 and 44, which require that the retroviral particles referred to in claims 7 and 8 can infect human melanoma cells, it is noted that it was known in the art that melanoma cells bind to RGD-ligands. See e.g., US 6,955,900, column 64, lines 1-4. Thus, chimeric retroviral particles comprising the nucleic acids suggested by the cited references would inherently bind to such cells.

Claims 41 and 43 read on embodiments of the claimed invention wherein the heterologous peptide is inserted at position 68 of the SU of the MLV ecotropic envelope protein. A translation of the SU nucleic acid of Figure 8 shows that position 68 of the SU lies in one of the two regions identified by Kingsman (Figure 2) as potential peptide insertion sites (i.e. position 68 of the SU MLV corresponds with the second Proline found in the second line of the alignment in Figure 2 of Kingsman). Thus, this position would have been an obvious point of insertion for the peptides.

Claim 42 reads on a retroviral particle comprising the nucleic acid of claim 1. Because the purpose of the modifications to the MLV protein in the cited references is to modify the tropism of chimeric retroviral particle, this claim is also obvious over the cited references.

16. **(Prior Rejection- Withdrawn)** Claim 38 was rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. (supra), in view of the teachings of Yamada et al. (Biochemistry 33:11678-83), and Curiel et al., (U.S. 2002/0081280). In view of the cancellation of this claim, the rejection is withdrawn.

Conclusion

17. No claims are allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is (571)272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachariah Lucas/
Primary Examiner, Art Unit 1648